BIOGRAPHICAL SKETCH

NAME: R. Julian Preston **POSITION TITLE:** Supervisory Environmental Health Scientist

Director, Environmental Carcinogenesis Division

EDUCATION/TRAINING:

Institution	Degree	Year	Field of Study
Peterhouse, Cambridge University (UK)	BA	1960-63	Genetics BHons.
Cambridge University (UK)	MA	1967	
Reading University (UK)	PhD	1970	Radiation Genetics

PROFESSIONAL EXPERIENCE:

1999-Present Director, Environmental Carcinogenesis Division, U.S. Environmental Protection Agency, RTP, NC.

1995-1999 Senior Scientific Advisor, Chemical Industry Institute of Toxicology, RTP, NC.

1992-Present Adjunct Professor, Department of Toxicology, North Carolina State University, Raleigh, NC.

1992-Present Adjunct Professor, Integrated Toxicology Program, Duke University, Durham, NC.

1991-1995 Department Head, Cellular and Molecular Toxicology, Chemical Industry Institute of Toxicology, RTP, NC.

1984-1991 Section Head, Biology Division, Oak Ridge National Laboratory, Oak Ridge, TN.

1978-1991 Senior Research Staff Member, Biology Division, Oak Ridge, TN.

1977-1982 Associate Director, University of Tennessee Biomedical Graduate School, Oak Ridge, TN.

1970-1991 Adjunct Professor, University of Tennessee Biomedical Graduate School, Oak Ridge, TN.

1970-1978 Research Staff Member, Biology Division, Oak Ridge National Laboratory, Oak Ridge, TN.

1963-1970 Staff Member, Medical Research Council Radiobiology Unit, Harwell, Didcot Oxfordshire, England Harwell, Didcot.

PROFESSIONAL SOCIETIES:

Editor, Mutation Research Letters -1980-1989; President, Environmental Mutagen Society B1989; Radiation Research Society B1973; Editorial Board of "Mutation Research" B1976; Environmental Mutagen Society B1978; American Society of Human Genetics B1987; Associate Editor, Environmental and Molecular Mutagenesis B1989; Associate Editor, Radiation Research -1990-1994; Associate Editor, Cell Biology and Toxicology B1990; Editorial Board, Analytical Biochemistry B1990; American Association for Cancer Research B1992; Health Physics Society B1997; Member, NIH Toxicology Study Section -1988-1992; Member, Committee I International Commission on Radiological Protection, 1993; Member, United States Delegation to the United Nations Scientific Committee on the Effects of Atomic Radiation -1997; Member of Board, National Council on Radiation and Measurements B1999.

SELECTED AWARDS AND HONORS:

Martin Marietta Technical Achievement Award B1985
Martin Marietta Technical Achievement Award B1989
Alexander Hollaender Award, EMS B1992
Lauriston S. Taylor Lecture, NCRP B2002

PUBLICATIONS (January 1, 1999 to present):

1. R.J. Preston, Incorporating Radiosensitive Subpopulations into Radiation Risk Estimates, Proceedings of the American Statistical Association Conference on Radiation and Health, San Diego, California, June 14-17, Radiat. Res., 151:100-101, 1998.
2. R.J. Preston, New Approaches in Genetic Toxicology and Their Possible Applications to Cancer Risk Assessment, CIIT Activities, 18(3):1-7, 1998.
3. R.J. Preston, Cytogenetic Effects of Ethylene Oxide, with an Emphasis on Population Monitoring, Critical Reviews in Toxicology, 29:263-282, 1999.
4. R. Julian Preston, Recent Advances in Genetic Toxicology and Their Relevance to Cancer Risk Assessment, Inhalation Toxicology, 11:555-557, 1999.
5. R.J. Preston, Chromosomal Changes. In Short/Medium Term Carcinogenicity Tests and Genetic and Related Effects. IARC Monoraph No. 146. International Agency for Research on Cancer, Lyon, pp 395-408, 1999.
6. R.J.M. Fry, U. Hagen, J. Kummermehr, R.J. Preston. Radiation. In: Toxicology, (Eds. Marquardt, H. Schafer, S.G. McClellan, R.O., and Welsch. F.) Academic Press, New York, pp. 937-958, 1999.
7. J.I. Everitt and R.J. Preston, Carcinogenicity and genotoxicity of inhaled substances. In: Toxicology of the Lung, 3rd Edition (Eds. D.E. Gardner, J.D. Crapo and R.O. McClellan), Taylor and Francis, Philadelphia, pp. 269-288, 1999.
8. T. Allio, E.M. Donner and R.J. Preston, A comparison of the roles of p53 mutation and AraC inhibition in the enhancement of bleomycin-induced chromatid aberrations in mouse and human cells, Mutat. Res. 447:227-237, 2000.
9. T. Allio and R.J. Preston, Increased sensitivity to chromatid aberration induction by bleomycin and neocarzinostatin results from alterations in a DNA damage response pathway, Mutat. Res. 453:5-15, 2000.
10. R.J. Preston, Incorporation of mechanistic data into cancer risk assessment. Mutation Research Forum, 5:1-4, 2000.
11. R. Julian Preston, Response to Klaunig, J.E. et al, Epigenetic Mechanisms of Chemical Carcinogenesis Commentary. Belle Newsletter, 9:38-40, 2000.
12. R. Julian Preston, Response to Klaunig, J.E. et al, Epigenetic Mechanisms of Chemical Carcinogenesis: Commentary, Human and Exper. Tox. 19:569-570, 2000.
13. R.J. Preston, Chapter 16. Genetic Toxicology In: Biochemical Toxicology (Eds. E. Hodgson and R. Smart). Wiley InterScience, pp. 397-413, 2001.
14. R. Julian Preston and G.R. Hoffmann, Genetic Toxicology, In, Casarett and Doull=s Toxicology (ed. C.D. Klaassen) McGraw Hill: York, PA., pp. 321-350, 2001.
15. R. Julian Preston, Summary and Conclusions for 21st Century Biodosimetry: Quantifying The Past And Predicting The Future, Radiation Protection Dosimetry, 97:75-77, 2001.
16. R. Julian Preston, Chapter 6. Chromosome Aberrations Induced by Low Doses and Low-Dose Rates of Ionizing Radiation, NCRP Report, 136:50-80, 2001.
17. R. Julian Preston, Quantitation of Molecular Endpoints for the Dose-Response Component of Cancer Risk Assessment, Toxicologic Path. 30:112-116, 2002.
18. R. Julian Preston (author) Operational Radiation Safety Program for Astronauts in Low-Earth Orbit: A Basic Framework. NCRP Report no. 142, NCRP: Bethesda MD, 2002.
19. R. Julian Preston, Mentors Are Made, Not Born, The Scientist, 16:54-55, 2002.
20. R. Julian Preston, Molecular Epidemiology: Potential Impacts on the Assessment of Public Health, Mutation Research, 543:121-124, 2003.
21. R.B. Conolly, J.S. Kimbell, D.B. Janszen, P.M. Schlosser, D. Kalisak, R.J. Preston, and F.J. Miller, Biologically motivated computational modeling of formaldehyde carcinogenicity in the F344 rat, Toxicol. Sci., 75:432-447, 2003.
22. C.N. Coleman, W.F. Blakely, J.R. Fike, T.J. Macvittie, N.F. Metting, J.B. Mitchell, J.E. Moulder, R.J. Preston, T.M. Seed, H.B. Stone, P.J. Tofilon, R.S. Wong, Molecular and cellular

biology of moderate-dose (1-10Gy) radiation and potential mechanisms of radiation protection: report of a workshop at Bethesda, Maryland, December 17-18, 2001. Radiat. Res. 159:812-834, 2003.
23. R. Julian Preston, LNT is the best we can do **B** to-day. J. Radiol. Protect. 23:263-268, 2003.
24. R. Julian Preston, 26th Lauriston S. Taylor Lecture: Developing mechanistic data for incorporation into cancer and genetic risk assessments: old problems and new approaches. Health Phys 85:4-22, 2003.
25. R. Julian Preston (an author), Assessment of Scientific Information for the Radiation Exposure Screening and Education Program: Interim Report. National Research Council, Washington, DC, 2003.
26. R. Julian Preston (author), Presidential Report on Radiation Protection Advice: Screening of Humans for Security Purposes Using Ionizing Radiation Scanning Systems. National Council on Radiation Protection, Bethesda, MD, 2003.
27. D.J. Brenner, R. Doll, D.T. Goodhead, E.J. Hall, C.E. Land, J.B. Little, J.H. Lubin, D.L. Preston, R.J. Preston, J.S. Puskin, E. Ron, R.K. Sachs, J.M. Samet, R.B. Setlow, and M. Zaider, Cancer risks attributable to low doses of ionizing radiation: Assessing what we really know. PNAS 100:24, 13761-13766, 2003.
28. R. Julian Preston. Children as a Sensitive Subpopulation for the Risk Assessment Process. Toxicol. Appl. Pharm. (in press), 2003.
29. L. Recio, M. Donner, D. Abernethy, L. Pluta, AM Steen, B.A. Wong, A. James, R.J. Preston. In Vivo Mutagenicity and Mutation Spectrum in the Bone Marrow and Testes of B6C3F1 LacI Transgenic Mice Following Inhalation Exposure to Ethylene Oxide. Mutagenesis (In Press).
30. R. Julian Preston. Children as a Sensitive Subpopulation for the Risk Assessment Process. Toxicol Appl. Pharm (In Press).

Research Interests Narrative: R. Julian Preston, Ph.D.
Mechanistic Data in Support of Cancer Risk Assessment

Past Research Activities

I spent a number of years at the Oak Ridge National Laboratory conducting research on the mechanisms of induction of chromosomal alterations and gene mutations by ionizing radiations and chemicals in somatic cells and germ cells. The major aims were to determine the relative roles of DNA misrepair and misreplication in the production of chromosomal alterations and to establish how such information might be incorporated into cancer and genetic risk assessment approaches. These mechanistic studies utilized novel approaches for addressing the hypotheses, in particular incorporating the use of DNA repair inhibitors, mutant cell lines and restriction enzymes. The research expanded into a consideration of how specific chromosome alterations could be induced (as opposed to just being selected for) and how such alterations could be used as predictors of cancer.

During the period I spent at the Chemical Industry of Toxicology, I conducted research on developing a database for cellular biomarkers of response that could be used as surrogates for cancer or birth defects allowing for their use in defining the nature of the cancer dose response curve at low doses. In addition, my research approaches incorporated studies to better understand the role of genetic susceptibility and sensitivity in the cancer risk assessment process. In particular, what is the potential magnitude of susceptibility to cancer induction, how did the magnitude vary with genotype and specific chemical exposures, and were high dose measures of sensitivity predictive of sensitivity at low doses.

Present Research Activities

During my appointment in the Environmental Carcinogenesis Division of NHEERL, I have been more involved in research oversight and setting longer-term directions. I have been particularly involved in establishing approaches for the incorporation of quantitative molecular data into the cancer risk assessment process. The aim is to select, or develop, informative biomarkers of cancer that can be used to not only define the nature of the cancer dose-response curve at low doses (qualitative assessment) but also to provide quantitative estimates of tumors at these same low doses. To do this it is essential to better understand the underlying mechanisms of tumors induced by environmental carcinogens and to better understand the mechanisms by which target organs or specific genotypes demonstrate chemical-specific sensitivities to tumor induction. In this regard, I have been directing the Division's efforts to establish the utility of functional genomics, proteomics and computational approaches together with expanding consideration of tissue responses for a more detailed understanding of the molecular basis for environmental carcinogenesis. I have also been involved in the development of a research program that is designed to address the question of whether or not early-life exposures result in an enhanced risk for the development of cancers during later life stages. A major aim of this effort is to determine if specific cellular housekeeping processes (e.g. DNA repair, DNA replication, cell cycle control and gene expression) are similar in the young as compared to older individuals and whether any observed differences could result in differential sensitivities to carcinogenesis from environmental exposures.

I have also expended efforts to establish how it might be possible to develop similar approaches for cancer risk assessment for ionizing radiations and chemicals whereby it might be more feasible to provide estimates of risk from combined exposures.

Future Research Activities

The current view of cancer induction is focused on the requirement for cells to develop a set ofsix required characteristics as defined by Hanahan and Weinberg. I plan to develop an experimental

approach using this information on acquired characteristics, to identify a suite of bioindicators that might be used as cancer predictors for use in dose-response characterization. This would provide more of a systems approach to describing cancer as opposed to a multi-step process. The approach would be to establish functional genomics and proteomics studies that would be based on phenotype as opposed to genotype. This type of approach could be applied eventually in a molecular epidemiology study for predicting public health risk that would be disease-based rather than risk-based for determining the impact of chemical exposures, and their regulation, on the health of a population.

My emphasis will remain on the use of quantitative mechanistic data for the assessment of health outcomes-linking risk and health status (prediction with validation) but taking advantage of computational and systems-based approaches. This is the most informative way to address the complex processes that constitute cancer development.